DETAILED ACTION

Summary

Receipt of Applicant's IDS filed on 01/08/10 is acknowledged. Receipt of Applicant's Response and Claim amendments filed on 01/07/10 is also acknowledged. Claims 89-112 are pending. Claims 89-112 are rejected.

Due to Applicant's claim amendments and arguments the 112 rejections of record are hereby withdrawn. All other rejections are hereby maintained.

MAINTAINED REJECTIONS

DOUBLE PATENTING

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 89-111 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-22 of U.S. Patent No. 7,544,370. Although the conflicting claims are not identical, they are not patentably distinct from each other because the both claim a method of producing, a product comprising a plurality of pantoprazole multiparticulates and pantoprazole multiparticulates with a spheroid core, initial seal coat, enteric coat, a diameter of 0.7-1.25mm, 25-30%microcrystalline cellulose, 4-6% polysorbate 80, 14-16% crospovidone, 0.5-2% hydroxypropyl methylcellulose, 5-8% sodium carbonate, and 1-2% water.

Claims 89-105 and 112 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21 of U.S. Patent No. 7,550,153 and claims 1-7 of U.S. Patent No. 7,553,498. Although the conflicting claims are not identical, they are not patentably distinct from each other because the both claim a method of producing, a product comprising a plurality of pantoprazole multiparticulates and pantoprazole multiparticulates with a spheroid core, initial seal coat, enteric coat, a diameter of 0.7-1.25mm, 25-30%microcrystalline cellulose, 4-6% polysorbate 80, 14-16% crospovidone, 0.5-2% hydroxypropyl methylcellulose, 5-8% sodium carbonate, and 1-2% water.

Response to Arguments

Applicant's agreed in their response to file terminal disclaimers over the above ODP rejections. The Examiner acknowledges this, however no such disclaimers have

been filed and as such the obviousness double patenting rejections of record are maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 89-112 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,753,265 ('265) in view of US 5,997,903 ('903) or in the alternative.

The instant claims are drawn to pantoprazole multiparticulates having reduced release under gastric conditions and fast release at neutral pH, wherein each of said multiparticulates comprises: a spheroid core consisting of about 20 % w/w to about 45% w/w of a pantoprazole salt or a hydrate thereof and one or more excipients comprising about 25% to about 30% w/w microcrystalline cellulose, about 4% to about 6% w/w polysorbate 80, about 14% to about 16% w/w crospovidone, about 0.5 to about 2% w/w hydroxypropyl methylcellulose, about 5% to about 8% w/w sodium carbonate, and about 1 to about 2 % w/w water; an initial seal coat comprising hydroxypropylmethyl cellulose on the spheroid core; and an enteric coat on the initial seal coat, wherein said multiparticulates have an average diameter of about 0.7 mm to about 1.25 ram.

- '265 teaches a dosage form of individual units or small beads, particles, pellets, etc of approximately 0.1 and 2 mm comprising a pantoprazole or salt thereof, surfactant, disintegrant, a separating layer, and an enteric coating made up of a copolymer of methacrylic acid and methacrylates (claims 1-3, 9-19 and col. 6, lines 7-9, 35-67-col. 7, lines 1-9 and 42-50).
- Examples 2-3, 10 and 12 specifically teach forming pantoprazole multiparticulate units of a size about 0.5 mm that are extruded, spheronized, and dried and then spray coating coated with a separating layer (which is hydroxypropyl methyl cellulose) and further an enteric coating (which is methacrylic acid copolymer). Example 2 also teaches polysorbate 80 and both examples teach including talc.
- '265 teaches a dosage form which can further comprise an overcoat on top of the enteric coating comprising hydroxylpropyl methyl cellulose and that the thickness of the overcoat is only limited by processing conditions (claim 8, col. 9, lines 6-30 and examples 9).
- '265 teaches that the enteric coating can be less than 60% of the total weight or at least 10 microns, preferably more than 20 microns thick (claim 6-7, col. 9, lines 1-5 and 45-48).
- '265 teaches that the core can contain hydroxylpropyl methylcellulose, microcrystalline cellulose, crospovidone, etc in the amounts as instant claimed (Examples 2-3, 10 and 12).
- '265 teaches the sodium salt of pantoprazole (col. 1, line 13-col. 3, line 42), sodium carbonate (col. 7, lines 15-20), hydroxypropyl methylcellulose, polyvinyl

pyrrolidone, etc (col. 6, lines 54-65) and sodium lauryl sulfate, polysorbate 80 (col, 6, lines 64-65 and examples).

- '265 teaches a suspension of multiparticulates, a divisible dosage form and a press through blister package of units (claims 9-10 and 20).
- '265 teaches that benzimidazoles are known to be anti-ulcers and decrease gastrointestinal acid secretion, treat non-ulcer dyspepsia, GERD, etc (col. 1, lines 23-30) (meeting the limitations of instant claim 112).
- '265 does not teach the amount of sodium carbonate or the amount of water instant claimed in claim 89. Further '265 does not teach the specific sodium sesquihydrate form of pantoprazole but does generically teach sodium salts, and enantiomers.
- '903 teaches a pantoprazole sodium sesquihydrate 29% wt. of core with crospovidone, fillers/binders such as HPMC, sodium carbonate in 6.5% wt., etc with an initial HPMC coat and a outer Eudragit coat and that having 1.5% water content wt does not discolor/decompose the dosage form (col. 2, lines 1-5, 21-25, 60-67 and Example 1)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make and use the multiparticulate dosage form of '265 in combination with '903. A skilled artisan would know how to substitute the specific pantoprazole of '903 (sodium sesquihydrate) for the generic pantoprazole including sodium salt and enantiomers of '265 for treating GERD among other things with predictable results. Further a skilled artisan would know how to formulate a dosage form product of '265

incorporating the techniques of '903 to include 1.5% water and 6.5% sodium carbonate. One of ordinary skill in the art would know how to optimize the ranges of '265 in view of '903, as the MPEP 2144.05 states "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."

Claims 89-112 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,159,499 ('499) and US 5,753,265 ('265) in view of 5,997,903 ('903).

- '499 teaches a composition and method of making the composition comprising a) a core of an acid labile benzimidazole active principle, b) an intermediate layer and c) an enteric layer, provided that the active is not omeprazole (abstract, claim 1). '499 teaches pantoprazole and a size of about 1 mm (claims 3-4, 8-9 and Examples 21-26).
- '499 Examples 21-26 teach hydroxypropylcellulose, polysorbate 80, crospovidone, sodium lauryl sulfate, talc, etc and enteric coat of methacrylic acid copolymer. All examples were made in the same way of Example 1 which states that the active suspension was sprayed onto a nuclei particle of 250 micron size and the core dried, and the temperature were kept below 45 degrees C, then the intermediate layer (hydroxypropylcellulose) added and then the enteric layer sprayed onto the core/intermediate layer.
- '499 teaches active principle in the amount of 2-50% (col. 7, lines 30-31 and 50-51).

- '499 teaches an intermediate layer of 5-30% (col. 7, line 25-26).
- '499 teaches an enteric coat comprising methacrylic acid copolymer (5-50 mg/per capsule), triethyl citrate (0-15 mg/per capsule), and talc (0-30 mg/per capsule, or 1-30% of the copolymer) (col. 7, lines 15-20 and 55-57).
- '499 teaches that the enteric coating can be 5-30% (col. 7, lines 27-28).
- '499 teaches that the microtablet core can contain hydroxylpropyl methylcellulose (1-100 mg/per capsule), crospovidone (0-50 mg/per capsule), polysorbate 80 or sodium lauryl sulfate (0-5.0 mg/per capsule), magnesium stearate (0.8-8), etc in the amounts as instant claimed (Examples 21-26; col. 6, lines 10-35; col. 7, lines 50-55).
- '499 teaches 40 mg of pantoprazole (Examples 6-8, and 21-26).
- '499 teaches multiple units in a capsule (claim 11, col. 7, lines 46-49).
- '499 teaches the active is useful for inhibiting gastric acid secretions in mammals and man, such as reflux esophagitis, gastritis, gastric ulcer, and duodenal ulcer, etc (col. 3, lines 44-54).
- '499 does not teach an example with microcrystalline cellulose, a suspension, foil pack or an final seal coat on the enteric coat, but does teach microcrystalline cellulose is a conventional excipient along with HPMC and crospovidone.
- '265 is taught above and teaches that the core can contain hydroxylpropyl methylcellulose, microcrystalline cellulose, crospovidone, etc in the amounts as instant claimed (Examples 2-3, 10 and 12).

- '265 teaches a dosage form which can further comprising an overcoat on top of the enteric coating comprising hydroxylpropyl methyl cellulose and that the thickness of the overcoat is only limited by processing conditions (claim 8, col. 9, lines 6-30 and examples 9).
- '265 teaches a suspension of multiparticulates, a divisible dosage form and a press through blister package of units (claims 9-10 and 20).
- '265 and '499 do not teach the amount of sodium carbonate or the amount of water instant claimed in claim 89. Further '265 or '499 do not teach the specific sodium sesquihydrate form of pantoprazole but do generically teach sodium salts, hydrates and enantiomers.
- '903 teaches a pantoprazole sodium sesquihydrate 29% wt. of core with crospovidone, fillers/binders such as HPMC, sodium carbonate in 6.5% wt., etc with an initial HPMC coat and a outer Eudragit coat and that having 1.5% water content wt does not discolor/decompose the dosage form (col. 2, lines 1-5, 21-25, 60-67 and Example 1)

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of '499, '265 in combination with '903. A skilled artisan would know how to substitute a combination of excipients including microcrystalline cellulose of '265, into the dosage form of '499 which teaches HPMC and crospovidone with predictable results since '499 also teaches that microcrystalline cellulose is a conventional excipient. A skilled artisan would know how to substitute the specific pantoprazole of '903 (sodium sesquihydrate) for the generic pantoprazole

including sodium salt, hydrates and enantiomers of '265 or '499 with predictable results. Further a skilled artisan would know how to formulate a dosage form product of '265 or '499 incorporating the techniques of '903 to include 1.5% water and 6.5% sodium carbonate. One of ordinary skill in the art would know how to optimize the ranges of '265 and '499 in view of '903, as the MPEP 2144.05 states "Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." One of ordinary skill in the art would have been motivated to combine the references and have reasonable expectation of success since all teach pantoprazole multiparticulate dosage forms comprising a core, intermediate layer and enteric coatings that are superior to previous pantoprazole formulations. '265 teaches that the composition can be formulated successfully into a suspension or foil pack and further that a final overcoat can be added and is advantageous to prevent agglomeration, protect from cracking, etc (col. 9, lines 25-28). Also the teaching of '265

Response to Arguments

Applicant's arguments with respect to the instant claims and the obviousness rejections of record are not persuasive. Applicant argues that (page 8 response):

> ...the application focuses on a multiple unit tableted dosage form, and in each of its working examples describes layering or spraying the active component onto a seed. Further, the '265 patent teaches compression of its "pellets" into a tablet. This is not an element of the invention claimed in the present application. The '265 patent contains no suggestion of multiparticulates having an extruded spheroid core composed of a pantoprazole compound and surfactant in the ratio recited in the present claims.

The Examiner respectfully points out that the instant claims do not require the core to be "an extruded spheroid core composed of a pantoprazole compound and surfactant" and not a "seed" core. Further, while '265 does teach using sugar sphere seed cores in Example 3 and it also teaches extrusion/spheronization of the active/excipients into a core of Example 2. Further, with respect to the surfactant and the ratio, claims 89, 100, 101 and 106 do not require surfactant; there is a limitation of polysorbate 80 in an amount of about 4% to about 6%, but, line 5 of claim 89 recites "**one** or more excipients" and accordingly independent claims 100, 101 and 106 also claim "one or more excipients". Accordingly, "one" can be any one of the excipients recited in claims 89, 100, 101, and 106, which does not have to be surfactant; '265 teaches Examples with microcrystalline cellulose, HPMC, etc in overlapping ranges in view of '903 which teaches sodium carbonate at 6.5% wt and 1.5% water which meets the limitations of the instant claims. Also the teaching of '265 "of its "pellets" into a tablet" is not a teaching away as prior to the compression into a tablet the pantoprazole pellets composition is known.

Applicant's arguments with respect to '499 and '265 in view of '903 are also not persuasive. Applicant's argue that there is no prima facie case of obviousness and no motivation to combine '499 and '265 in view of '903, and the examiner respectfully points out that applicant's argue against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Simply because '499 teaches that it distinguishable over '265 is not a teaching away, as the combination of '499 and '265 in view of '903 is not related to the excluded alkaline compounds and mannitol as taught by '499; but rather '265 is relied upon to show substitution of microcrystalline cellulose a known excipient (as suggested by '499) into the core of '499 would be obvious and further '265 teach an overcoat on the cores of HPMC, suspensions of multiparticulates and blister packs, etc are advantageous. Again Applicant's arguments with respect to the surfactant are not persuasive as it is not a required element of the instant claims which claim "one or more excipients". Further, the rejection is based on '499 and '265 in view of '903, wherein '903 is relied upon to show that substitution into the product of '499 and '265 of generic pantoprazole for the specific pantoprazole sodium sesquihydrate of '903 is within the purview of the skilled artisan and would yield predictable results. And '903 also teaches the known technique of formulating using amounts of sodium carbonate and water as instant claimed and the combination with the known product of '499 and '265 ready for improvement is within the purview of the skilled artisan and would yield predictable results.

Conclusions

Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bethany Barham whose telephone number is (571)272-6175. The examiner can normally be reached on M-F, 8:30 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax can be reached on 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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